

Metastatic Carcinoma Masquerading as Primary Thyroid Cancer: *

A Report of Authors' 14 Cases

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THE THYROID GLAND is not frequently the site of primary cancer. It is perhaps even less frequently the site of metastatic cancer. In a series of 1,000 consecutive and unselected autopsies performed at the Mayo Clinic, reported by Mortensen, Woolner and Bennett,²⁸ 467 had, or previously had had, malignant neoplasms. Of these, 370 had metastases demonstrated. In 18 cases, i.e., 3.9 per cent of all patients with malignant neoplasms, there was secondary disease of the thyroid gland. This is a low incidence. Because of the interest at the Mayo Clinic in thyroid disease, this is probably a valid figure based on more careful study than the usual cursory palpation and random sample, often taken with the gland *in situ*, at postmortem examinations. These instances of secondary carcinoma were discovered only after a most complete and careful examination of each individual gland, both macroscopically and microscopically. The incidence quoted by Willis in his comparable personal series of 500 cases is 4 per cent.⁴⁰ His interest in the spread of tumors is widely known.

Six of the 18 thyroid glands involved in secondary cancer in the Mayo series were not comparable to the group which we are reporting. In five of them the secondary cancer was lymphoid in origin and in one it was a direct spread from the larynx. More surprising is the Mayo figure of 28 primary carcinomas of the gland found in this series. Only one of these was a clinical carcinoma and in this case the diagnosis had been made before death and the thyroid cancer was the cause of death. All the metastatic carcinomas, and all the other primary carcinomas were "pathologists' cancers," not clinical cancers, and none of the metastases presented as goiters. The metastatic carcinomas to the thyroid reported in the literature^{1, 20, 26, 28, 32, 35, 38, 39, 40} as incidental autopsy findings, together with 43 found in 7,382 consecutive autopsies at the Presbyterian Hospital,²² are listed according to primary sites in Table 1.

TABLE 1. *Metastatic Carcinoma in Thyroid—
Incidental Autopsy Findings*

Breast	64	Epidermoid	8
Lung	62	Pancreas	5
Melanoma	25	Uterus	5
Kidney	24	Liver and bile ducts	3
G.I.	20	Miscellaneous	37*
Total cases 253			

* 2 each: Prostate, ovary and chorio-epithelioma.
1 each: Cervix, adrenal, parotid, bladder, chordoma.
26 not specified.

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TABLE 2. *Metastatic Carincoma in
Thyroid—Clinical Cases*

Primary Site	Cases in Literature (1934–58)	Authors’ Cases (1949–58)	Total Cases
Kidney	30	3	33
G.I. tract	7	2	9
Lung	3	4	7
Breast	2	4	6
Adrenal	1	0	1
Liver	1	0	1
Skin	0	1	1
	44*	14**	58

* 39 surgical, 5 autopsy (3 kidney, 2 G.I. tract).
** All surgical.

While secondary malignant involvement of the thyroid from a distant focus is uncommon and often difficult to recognize clinically, it is not too unusual for this organ to be directly involved by squamous cell carcinoma which has taken origin in head and neck organs—often the larynx. Willis³⁸ points out that direct extension can take place from the primary site, or from metastatic disease in the regional lymph nodes. He cites a remarkable case in which “extensive cervical metastases from a small lingual carcinoma had almost completely destroyed the gland, and compensatory hyperplasia of an accessory lingual thyroid had occurred.” With involvement by direct extension there usually is little doubt about the nature of the thyroid involvement prior to operation, even less at the time of actual surgery, and there should be none on the pathologist’s study of the surgical specimen. This type of case has not been included in the present report which deals only with metastatic involvement in which the diagnosis generally is less obvious.

It happens occasionally that a patient is operated upon with the presumptive diagnosis of primary thyroid carcinoma, and the secondary nature of the neoplasm is only recognized subsequently. At times the correct diagnosis does not become apparent for months or even years later, as in one of our own cases with primary

disease in the kidney. In the meantime, the patient may be subjected to additional surgical and other therapeutic procedures which, in the light of the correct diagnosis, are unjustified and regrettable. The clinical cases from the literature,^{2, 3, 5–11, 13–19, 21, 23, 24, 26, 27, 30, 31, 33, 34, 36, 37} together with the authors’ surgical cases, are listed in Table 2.

In a review of the surgical experiences at the Presbyterian Hospital, 14 masquerades have come to light—i.e., metastatic tumors of the thyroid gland simulating primary disease. This figure is to be compared with somewhat more than 500 cases of thyroid cancer. The spread of the disease to the gland was considered either retrograde lymphatic or blood-borne, or both.

Of the 14 cases, eight were women and six were men (Table 3). The patients’ ages ranged from 34 to 67 years. The cases fall naturally into four groups according to primary site of tumor: Group I: four patients with primary tumor of the breast; Group II: four patients with primary tumor of the lung; Group III: three patients with primary tumor of the kidney; and Group IV: miscellaneous primary sites—rectum, gastrointestinal tract (or pancreas), and squamous cell epithelioma of the leg. These four groups are presented in the form of brief case analyses with an accompanying table and comment.

**Group I—Primary Tumors of Breast—
Case Analyses**

Case 1. N. B. A 57-year-old housewife hospitalized for left-sided seizures of one year’s duration. Episodes of vertigo without loss of consciousness for the previous 5 years. Carcinoma of left breast treated elsewhere by simple mastectomy and radiotherapy two years before admission. Fetal adenoma of thyroid removed 23 years previously.

Admission work-up revealed an enlarged firm thyroid remnant on right and a supraclavicular mass on left. X-rays of chest and skeleton negative. No local recurrence of breast cancer. Opinion favored metastatic breast cancer in brain, thyroid, cervical lymph nodes. Possibility of primary thy-

TABLE 3. *Metastatic Carcinoma of Thyroid—Authors' 14 Surgical Cases*

Patient Name	Sex	Primary	Preoperative Diagnosis	Surgical Pathologist Diagnosis	Operation
N.B.	F	Breast	2° Ca. ? 1° Ca.	2° Ca.	Biopsy
J.D.L.	F	Breast	1° Ca.	1° Ca.	"Total"
G.W.	F	Breast	Equivocal	F.S.—itis P.S.—2° Ca.	Biopsy
M.V.D.	F	Breast	1° Ca.	1° Ca.	Total+rad. neck medias.
M.M.	M	Lung	? 2° Ca. ? 1° Ca.	? 1° Ca.	Lobectomy
J.S.	M	Lung	1° Ca.	2° Ca.	Total and L.N.
M.B.	F	Lung	? 1° Ca.	F.S.—1° Ca. P.S.—2° Ca.	Total
A.C.	M	Lung	2° Ca. ?—itis	2° Ca.	Biopsy + isthmect.
S.S.	F	Kidney	? 1° Ca. ? Hodgkins	2° Ca.	Partial "N.T.N.G."
L.S.	F	Kidney	N.T.N.G. Ca. Lung	1° Ca.	Total, L.N. + medias.
H.P.	M	Kidney	? 2° Ca. ? 1° Ca.	2° Ca.	Lobectomy
V.C.	F	Rectum	1° Ca.	F.S. 1° Ca. P.S. 2° Ca.	Total
H.S.	M	G.I. or pancreas	1° Ca.	2° Ca.	Biopsy
M.T.	M	Skin	?—itis ? 2° Ca.	2° Ca.	Lobectomy

F.S.—Frozen section; P.S.—Permanent section.

roid carcinoma raised because of previous adenoma. Operation advised to rule this out.

Operation (2/16/55). Exploration, biopsy, right lobe of thyroid, and left supraclavicular lymph node. No frozen section. Tissue diagnosis metastatic breast cancer.

Course. Uneventful recovery from operation. Died at home three months later. No autopsy.

Summary. Carcinoma of breast metastatic to brain, thyroid, cervical lymph glands. Neck explored because of previous documented thyroid adenoma. Biopsies only. No diagnostic errors.

Case 2. J. D. L. A 47-year-old colored woman, a houseworker, with nodule in left lobe of thyroid for two years and a rapidly enlarging mass in left neck for 3 weeks. Normal chest x-ray, skeletal survey and esophagram. *Breast examinations repeatedly negative.* Preoperative diagnosis by most observers was primary thyroid cancer. Senior surgical

consultant raised question of secondary malignancy because of peculiar consistency of neck mass and recent personal case of masquerade.

Operation (5/28/56). Biopsy cervical lymph node, left, and *left lobectomy*. Total not done because of unexpected right-sided fixed superior mediastinal mass. Frozen section diagnosis on lymph node: Anaplastic carcinoma, site undetermined. Permanent section diagnosis: Carcinoma, Hürthle cell type, of thyroid. Eight months *after* operation two small masses discovered in right breast. Biopsy revealed primary breast cancer similar, histologically, to tumor in thyroid and cervical nodes. Case reviewed and diagnosis changed by surgical pathologist.

Summary. Unsuccessful attempt to remove metastatic thyroid tumor mistaken for primary cancer. True primary did not appear until eight months after operation, and was in the *right breast*. Errors in diagnosis both by clinicians and

surgical pathologists. Death 28 months after operation with disseminated disease. No autopsy.

Case 3. G. W. A 61-year-old woman with carcinoma of the left breast and axillary metastases treated elsewhere by radical mastectomy and post-operative x-ray. No local recurrence. No evident lung metastases. Eight years later had dysphagia, pain in the left neck and weight loss. Treated by x-ray without relief.

Preoperative work-up led to varying diagnoses. Internist and radiologist inclined to favor metastatic disease, ruling out thyroiditis because of a normal radio-iodine uptake. Surgeon thought the diagnosis lay between primary thyroid carcinoma and thyroiditis.

Operation (6/17/57). Exploration, biopsy of tumor in upper anterior mediastinum and of tumor in left lobe of the thyroid. Quick frozen section diagnosis at the time of operation: Thyroiditis. Permanent sections showed adenocarcinoma with some mucin-containing cells. Final Diagnosis: Carcinoma of thyroid and mediastinal lymph node following carcinoma of breast.

Summary. Operation undertaken to establish diagnosis. Error on immediate frozen section. Biopsy only. Patient died 18 months after biopsy, 9½ years after mastectomy. No autopsy.

Case 4. M. V. D. A 41-year-old housewife with recurrent goiter, progressive hoarseness and dysphagia of 4 months' duration. Two operations three years previously: 1) Biopsy of thyroid; 2) "Total" thyroidectomy for "adenoma malignum" (both operations at another hospital). Sections from second operation reviewed in Department of Surgical Pathology and diagnosis erroneously confirmed.

Preoperative work-up: Scintiscan uptake of 19 per cent concentrated at left upper pole. X-ray: negative skeletal survey; right hilar lymphadenopathy. Esophagram indicated encroachment on trachea and cervical esophagus. Diagnosis: recurrent thyroid cancer.

Operation (7/6/57). Total thyroidectomy with dissection of left neck and mediastinum. Sections from thyroid considered primary carcinoma, Hürthle cell type. Review of lymph nodes after clearing suggested possibility of primary breast lesion. Breasts re-examined, no tumor found. Second operation (8/20/57), right neck dissection.

Course. Four months after admission retraction sign in left breast, but no mass. Biopsy, (11/8/57) positive for primary mammary lesions, after many sections finally revealed intraductal carcinoma. Death two months later. No necropsy.

Summary. Presumably documented adenoma malignum erroneously led to interpretation that in-

creasing mass beneath thyroidectomy scars was recurrence. Pathologist's error and delayed appearance of anaplastic breast cancer resulted in extensive major surgery (two procedures).

Comment

Two of the four cases were particularly puzzling. In J. D. L. and M. V. D. clinical evidence of a breast lesion did not become apparent until eight months and three months respectively, *after* thyroid surgery. In each instance the breasts had been examined before operation by experienced clinicians. Even so, one observer had doubts about J. D. L. Moreover, because the second patient, M. V. D., with one of these cryptic lesions was studied after the primary breast tumor had finally been found in the case of J. D. L. and because the metastatic tumors in the thyroid in each case were characterized by acidophilic cells suggesting Hürthle cell carcinoma, the pathologist's suspicions were aroused. The physical examination of the breasts of M. V. D. was, therefore, immediately repeated before further definitive surgical procedures were undertaken. This patient's breasts were small and not hard to examine. There was no evidence whatsoever of a primary mammary neoplasm at this time.

In the other two patients in this group, M. B. and G. W., the diagnosis of breast cancer had been documented surgically two years and eight years respectively before operation on the thyroid gland was undertaken. The possibility that the enlargement of the thyroid gland was due to mammary cancer was entertained prior to exploratory operation in both patients. Most observers, however, felt that a primary thyroid lesion was sufficiently likely to justify exploration of the neck, particularly in the case of N. B. who had had a thyroid adenoma removed 23 years earlier. On exploration and biopsy in this case, N. B., the diagnosis was apparent to the surgical pathologist on frozen section. On biopsy of the other case, G. W., in which a second possible clinical diagno-

sis was thyroiditis, the frozen section diagnosis was interpreted as thyroiditis, which may have saved the patient from more radical surgery. Later, the permanent sections showed metastatic carcinoma.

Group II—Primary Tumors of Lung— Case Analyses

Case 1. M. M. A 64-year-old man, a heavy smoker, with a chief complaint of dyspnea and wheezing in chest for four months. Otherwise well.

Physical Examination. Hard mass in right lobe of thyroid with bilateral, small, firm supraclavicular lymph nodes. Chest x-ray showed density in right upper lobe with smaller nodules both upper lung fields. Bronchoscopy and Papanicolaou smear negative. Preoperative diagnosis: Carcinoma, primary, either in lung or in thyroid.

Operation (8/19/49). Biopsy of lymph node, frozen section, right thyroid lobectomy. Diagnosis: Primary carcinoma, ? Grade III. Permanent sections diagnosis: Carcinoma of thyroid following carcinoma of ? lung.

Course. Uneventful postoperative course. Died 1–2 years after operation. No record of autopsy.

Summary. Carcinoma of lung metastatic to thyroid and supraclavicular lymph nodes. Frozen section diagnostic error, led to right thyroid lobectomy.

Case 2. J. S. A 60-year-old man with a 3-month history of crippling low-back pain with radiation down legs. Stony hard, 3 cm. nodule in right lobe of thyroid, not noticed by patient. Enlarged, firm, right axillary lymph nodes. X-ray showed osteolytic areas in sternum, 4th lumbar vertebra and both iliac bones. Chest clear 2 weeks before operation. Preoperative diagnosis: Carcinoma of thyroid with metastases to axillary lymph nodes and bone.

Operation (11/15/50). Total thyroidectomy with pretracheal node and right axillary lymph node dissection. No biopsy. No frozen section. Surgical pathology diagnosis: Nontoxic nodular goiter. Carcinoma of pretracheal and right axillary lymph glands following carcinoma of unknown origin (lung?). Later, one microscopic metastasis found in thyroid, not a dominant nodule. X-ray one month after operation showed probable atelectasis of left upper lobe and questionable "intrapulmonary lesion." Decompression laminectomy L 2–3 and L 4–5 and palliative x-ray therapy given without benefit. Progressive downhill course. Died 7 months after operation of sudden atelectasis during bronchoscopy done in attempt to locate primary. No autopsy.

Summary. Single thyroid nodule strongly suggestive, clinically, of primary thyroid cancer. Chest plate clear 15 days before operation, misleading. Biopsy and frozen section might have been informative. Apparent tumor of thyroid actually nontoxic nodular goiter. Primary in lung never proved, although subsequent chest x-rays and microscopic findings were suggestive.

Case 3. M. B. A 67-year-old housewife, non-smoker, with gradually enlarging goiter for one year and one month of progressive dyspnea, substernal pain and cough.

Physical Examination. Advanced malignant disease with hard nodular thyroid and fixed left supraclavicular nodes. X-ray evidence of extensive multiple pulmonary metastases and fluid at left base. Skeletal survey negative. Preoperative diagnosis of probable primary thyroid cancer; possibility of primary lung tumor also considered. Planned to treat with total thyroidectomy, followed by therapeutic I_{131} for metastases if biopsy positive.

Operation (1/21/54). Biopsy lymph node. Frozen section "carcinoma." Total thyroidectomy. Permanent sections: mucin-producing carcinoma suggesting lung.

Course. Died 9th postoperative day.

Autopsy. Mucin-secreting adenocarcinoma of lung with widespread metastases including thyroid.

Summary. Frozen section error on lymph node biopsy. Total thyroidectomy then performed as preliminary to possible treatment of lung lesions with I_{131} . Autopsy confirmed final surgical-pathology diagnosis.

Case 4. A. C. A 34-year-old man with enlarged lymph nodes in the right neck for one year. Chest x-ray suggested localized pneumonitis in right mid-lung field. Cervical node biopsy showed metastatic squamous cell carcinoma. Bronchoscopy negative. Because of rapid enlargement of thyroid, exploration advised to establish diagnosis and to relieve pressure. Preoperative diagnosis: metastatic bronchogenic cancer.

Operation (10/15/54). Exploratory with removal of thyroid isthmus. Frozen section and permanent sections confirmed original diagnosis of metastatic squamous cell carcinoma.

Course. Died of disease elsewhere 3 months later. No autopsy.

Summary. Operation undertaken to relieve pressure and establish diagnosis. Isthmectomy only. X-ray changes presumptive evidence of primary lung cancer.

Comment

In only one of these four cases (J. S.) was there a real masquerade. The negative

chest x-ray prior to operation was misleading. The bone metastases and the stony-hard nodule in the thyroid were entirely consistent with primary thyroid carcinoma. So was the pretracheal lymph node involvement. These nodes were presumably the source of the microscopic metastasis (not a "masquerading" metastasis), having acted as secondary distributing foci to the nontoxic nodular goiter. The axillary metastases, on the other hand, might have aroused suspicion, in the absence of clinically-palpable cervical lymph-node involvement. Biopsy of these might have been helpful. Axillary masses in thyroid carcinomas are extremely unusual. The one instance in our experience which before operation was thought to be axillary metastasis proved to be direct extension to the axilla from metastatic thyroid carcinoma in the lung, not true lymph-node metastasis. Biopsy and frozen section of the nontoxic nodular goiter at the time of operation also might have been rewarding. No real palliation was achieved in this case by radical attack on the thyroid although this was true in some other cases in the series.

The pathologist led the surgeon astray twice on frozen section at the time of operation. In the first case (M. M.) this led to a lobectomy, and in the third case (M. B.) to a total thyroidectomy. This third case, however, involved a desperately-ill patient, operated upon in the faint hope that the remote possibility of primary thyroid cancer might prove true, and that the extensive disease in the lungs might be functionally active. These could then, perhaps, have been temporarily arrested by radio-iodine therapy. This case survived only nine days. The final diagnosis by the surgical pathologist was verified by postmortem examination.

In the other three cases the primary disease in the lungs was not documented by autopsy nor by biopsy. However, the presumptive diagnosis was strongly suggested by the x-ray findings and the surgical pa-

thologist's final report. Well differentiated squamous cell carcinoma in the thyroid should not lead the surgical pathologist to make a diagnosis of thyroid carcinoma, even if the primary focus remains cryptic for a long time. It is the less differentiated carcinomas of the lung which may lead the pathologists astray. Removal of the isthmus of the thyroid in the fourth case (A. C.), after frozen section diagnosis had confirmed the clinical impression, facilitated later mandatory tracheostomy, and did not constitute unnecessary radical surgery.

Group III—Primary Tumors of Kidney— Case Analyses

Case 1. S. S. A 61-year-old housewife admitted with fever and mental confusion. She had had a mass in the neck for 5 years. Right nephrectomy elsewhere 14 years previously for clear cell tumor of the kidney. Examination: A chronically-ill woman with firm nodular goiter, most marked on left. Daily spiking of fever to 38.8° C. for four weeks with marked disorientation. X-rays: lungs clear; trachea deviated. Alkaline phosphatase 16.6 and 17.2 Bodansky units per cent. Secondary anemia. E. S. R. 120. Preoperative diagnosis: ? primary thyroid carcinoma with central necrosis; ? Hodgkin's disease of thyroid.

Operation (2/16/50). Partial thyroidectomy. Pathology at operation thought to be nontoxic nodular goiter. No frozen section. Prompt subsidence of fever and mental confusion postoperatively. Surgical pathology diagnosis: Carcinoma of thyroid following carcinoma of kidney; nontoxic nodular goiter.

Course. Three years later explored for retroperitoneal recurrence of original tumor. Died five years after thyroidectomy. No autopsy.

Summary. Partial thyroidectomy immediately controlled fever and disorientation in patient with thyroid metastases from primary kidney tumor removed 14 years previously. No recurrence of metastatic goiter—a good palliative result. Clinical diagnostic error. Long course of renal carcinoma (19 years from nephrectomy to death).

Case 2. L. S. A 48-year-old housewife with cough and dyspnea of 3 months' duration, referred because x-ray shadow suspicious of neoplasm in right lung discovered by Board of Health. Incidental history of goiter for 8 years with recent rapid increase in size. Work-up revealed mass in left lobe of thyroid dipping below clavicle. X-rays

indicated substernal goiter, with deviation and compression of trachea; also right hilar mass. Bronchoscopy and Papanicolaou smear negative. Two preoperative diagnoses: Nontoxic nodular goiter, substernal; primary carcinoma of lung. Thyroidectomy was planned as a first step to avoid airway difficulties when lung was resected.

First Operation (5/28/51). Left subtotal lobectomy with removal of substernal mass. Surgical pathology diagnosis: Adenoma malignum and nontoxic nodular goiter.

Second Operation (6/21/51). Exploratory thoracotomy for removal of "solitary lung metastasis." Mass proved to be large hilar lymph node. Surgical pathology diagnosis: Carcinoma of hilar node following carcinoma of thyroid.

Third Operation (8/17/51). Total thyroidectomy and mediastinal dissection. Surgical pathology diagnosis: Nontoxic nodular goiter. No mediastinal lymph-node metastases.

Course. Exploratory laparotomy three years later elsewhere. Findings: Metastases to right ureter from clear cell carcinoma left kidney. Final amended diagnosis: Carcinoma of thyroid and hilar lymph node following carcinoma of kidney. Death four and one-half years after thyroidectomy. No autopsy.

Summary. Error in x-ray interpretation of pulmonary lesions. Three major operations. Two surgical pathology errors not discovered until tissue diagnosis made after a fourth operation, three years later, at another hospital.

Case 3. H. P. A 63-year-old man admitted with a firm mass in left lobe of thyroid. Pedunculated lesion of right axilla removed three and one-half years earlier interpreted as metastasis from probable kidney tumor. Right nephrectomy, (10/1/54) confirmed diagnosis. Metastasis in scalp removed two and one-half years later. Scintiscan revealed thyroid nodule to be "cold." Preoperative diagnosis: metastasis to thyroid from hypernephroma. Surgeon believed operation indicated for diagnosis (? primary thyroid) and to forestall development of obstruction.

Operation (7/8/58). Left complete thyroid lobectomy. Frozen section and permanent sections: metastasis from renal carcinoma.

Course. Admitted for terminal care to another institution, nine months post-thyroidectomy with metastases in lung and bone.

Summary. Lobe of thyroid containing metastatic nodule from renal carcinoma removed to forestall respiratory obstruction and to confirm diagnosis. No clinical or pathological errors. Thyroid metastasis a clinical goiter.

Comment

Two of these three cases were real masquerades, baffling clinicians, radiologists and surgical pathologists. In the first case the preferred diagnosis was primary carcinoma of the thyroid. The surgeon was led astray by the gross appearance of the gland at operation. The diagnosis by the surgical pathologist was correct and later confirmed by comparing sections from the primary tumor. There was no local recurrence of metastatic disease in the neck and we believe thyroidectomy was justified and gave palliation during the five years of survival.

In the second case the thyroidectomy was done for a large goiter, not considered neoplastic, so that subsequent thoracotomy for a supposed solitary primary lung lesion would be safe from airway complications after operation. The error in the surgical pathologist's interpretation of thyroid tumor as primary did not avert the thoracotomy which was done for removal of a solitary intrapulmonary metastasis. The hilar mass found instead seemed to be a natural lymph-node metastasis. The pathologist's diagnostic error was compounded, and led to mediastinal dissection. There is a real pitfall for pathologists in differentiating between primary and metastatic clear cell carcinomas of the thyroid. That these tumors can be primary has long been known, but they give pause. Recently, functional lymph-node metastases have been demonstrated by radioautography in follicles lined by the controversial clear cells.

In the third case the lobectomy seemed justified because of anticipation of possible obstructive symptoms.

As has been pointed out by Denton and McClintock,¹⁵ one of the outstanding features of this type of case may be the length of time which elapses between the removal of the renal tumor and the documentation of metastatic disease in the thyroid. These authors report one case of their own and five in the literature in which from seven

to 13 years elapsed following nephrectomy for carcinoma before the metastases to the thyroid were recognized for what they really were. In one of our cases (S. S.), there was an interval of 14 years between nephrectomy and thyroidectomy.

It is interesting that among the case reports in the literature of patients who on surgical exploration were found to have metastatic disease in the thyroid gland, the kidney is cited as the primary source somewhat more than three times as frequently as any other organ (Table 2). As a primary source of incidental metastases found at autopsy, the kidney does not rate as high on the list (Table 1).

Group IV—Primary Tumors of Miscellaneous Sites—Case Analyses

Case 1. V. C. A 56-year-old medical secretary with stony-hard, rapidly enlarging thyroid mass and later development of satellite lymph nodes, diagnosed preoperatively as primary carcinoma with lymph-node metastasis.

Operation (12/11/52). Biopsy of lymph node. Frozen section. Diagnosis apparently confirmed. Total thyroidectomy. Bilateral radical neck dissection planned. Permanent sections showed mucin-producing tumor suggesting large bowel origin, and also Hashimoto's thyroiditis. Primary found postoperatively on proctoscopy 13 cm. from anal orifice. History of rectal bleeding not mentioned by patient because of reassuringly "negative" proctoscopy elsewhere 7 months earlier. Palliative anterior resection (12/22/52): Extensive involvement of retroperitoneal lymphatics; direct invasion of many mesenteric veins. Death from cerebral metastases 3 months later.

Summary. Unrecognized rectal cancer metastasized to thyroid gland which acted as secondary distributing focus to cervical nodes in pattern characteristic of primary thyroid cancer. Error in frozen section diagnosis. Preoperative and operative clinical diagnostic errors caused in part by "negative" proctoscopy and pattern of cervical lymphatic involvement. Autopsy elsewhere confirmatory.

Case 2. H. S. A 58-year-old business man with progressive weight loss and fatigue of six months duration and recent sore throat and hoarseness. Physical examination indicated far-advanced malignancy with nodules over calvarium, nodular liver and hard fixed mass in left lobe of thyroid. X-ray:

negative chest; translucencies in skull. Primary site thought to be probably thyroid, although metastatic involvement considered also because of disseminated disease and liver involvement.

Operation (8/6/53). Biopsy of left lobe of thyroid. Surgical pathology diagnosis: Carcinoma of thyroid following carcinoma unknown origin—? G.I. tract or pancreas. Patient died 3 weeks later.

Summary. Operation undertaken to establish diagnosis. Biopsy only. Rapidly fatal course—7 months, perhaps less suggestive of primary in G.I. tract than of primary in pancreas.

Case 3. M. T. A 38-year-old man with sudden onset of tender enlargement of right lobe of thyroid. Chronic osteomyelitis of left leg following injury 26 years previously. Multiple skin grafting procedures to infected area, with ultimate development of squamous cell epithelioma in scars. Disarticulation of leg at hip with retroperitoneal lymph-node dissection. Specimen revealed involvement of inguinal and external iliac glands. In addition to the tenderness of the right lobe of thyroid, pain radiated up to chin and left ear. Skeletal survey and chest films negative. Acute thyroiditis considered most likely, though possibility of metastatic disease in gland also considered.

Operation (3/7/57). Biopsy lymph node. Frozen section showed squamous cell epithelioma. Right lobectomy to clear trachea. Successful for 2 months when tracheostomy necessary.

Course. Succumbed to disease 4 months after thyroidectomy. No autopsy.

Summary. Squamous cell epithelioma in old scar of leg metastasized to thyroid—mimicking acute thyroiditis. Operation for diagnosis: Lobectomy to clear trachea.

Comment

Group IV is not a group at all, but three miscellaneous cases, put together for convenience. The first case, which was dramatic enough to impress all the members of the Thyroid Clinic and the Department of Surgical Pathology, is an almost perfect masquerade (except in hindsight!). Moreover, we only know of four other surgical cases in which the primary tumor was in the rectum (Mayo and Schlicke²⁸—1; Cope *et al.*¹²—2; Bruce and Michie¹⁰—1). The last authors also report a surgical case with the primary in the colon. Two other cases with clinical involvement of the thyroid shown at autopsy to have come from pri-

mary colon tumors are those of Rankin and Fortune³¹ and of Sklaroff.³⁴ Incidental autopsy findings of metastases to the thyroid from the colon and rectum are also scarce, i.e., six reported from the colon and only two from the rectum. The Presbyterian Hospital case with metastases to the thyroid from the rectum had cervical lymph-node involvement on the ipsilateral side, clinically strongly suggestive of primary thyroid origin. Later, when palliative anterior resection was performed, the rectal tumor was found to invade the superior hemorrhoidal veins for a considerable distance. There was extensive involvement also of the retroperitoneal lymph nodes. The cervical nodes were interpreted as metastases from the metastatic tumor in the thyroid acting as a secondary distributing focus. The cerebral metastases may have reached the brain by way of the vertebral system of veins described by Batson.⁴

In reviewing the second case it is interesting to speculate as to the possible primary source. The gastro-intestinal studies were essentially negative in this patient, and there was nothing suggestive in the clinical course to implicate this system. The best indication, therefore, that we have as to the possible source of this mucin-producing adenocarcinoma is the short postoperative course. This makes a silent carcinoma of the pancreas the best guess statistically, but it is only a guess. However, the histopathology was consistent with primary pancreatic carcinoma, though not diagnostic.

The third case is perhaps unique, although Willis³⁹ mentions metastases to the thyroid from skin cancers, as incidental findings at autopsy. We know of no other case reported in which squamous cell carcinoma of the skin of the *leg* has metastasized to the thyroid. It is also interesting that this metastasis caused such an extreme degree of pain that acute thyroiditis was considered as a possible diagnosis.

Discussion

The dubious distinction of having, perhaps, the largest series of this kind yet to be reported caused us to hesitate a little in making this public confession. The number of mistaken preoperative diagnoses and of misleading interpretations of the histopathology reflect no glory as far as our diagnostic acumen is concerned. Ten years ago, Cope¹² and associates reported their surgical cases in a paper presented at the annual meeting of the American Goiter Association. When this was published the title was "What Thyroid Nodules Are to Be Feared," and the running head for subsequent pages was "*Dangerous Thyroid Nodules.*" The latter seems to us a highly appropriate title. It is of some comfort to us to learn that members of other thyroid clinics, to which, inevitably, difficult problems and cases of advanced disease are referred, have had the same experience as we have had. However, from such experience they and we have learned a good deal. It seemed worthwhile to share this knowledge and the cases seem to us of considerable interest.

The radical procedures we have listed (Table 3) stem from our policy of what we consider to be the safest approach to the thyroid nodule which is suspect clinically—particularly the single nodule. We have seen enough implants of primary thyroid carcinoma—particularly of the papillary type—to deplore open biopsy on the primary tumor. If there are no clinically suspicious lymph nodes when the thyroid is exposed, we have made it a practice to perform a lobectomy and to present the lobe as the biopsy specimen for immediate examination by the surgical pathologist. The paraglandular and pretracheal lymph-node-bearing tissue should be part of the specimen. If the pathologist can make a positive diagnosis of carcinoma at the time of operation, particularly if it is papillary carcinoma, a total thyroidectomy can be

completed at that sitting. Further node dissection is undertaken according to the findings in the lymph nodes and in the opposite lobe.

When suspicious lymph nodes are found at operation, one of these usually constitutes the biopsy specimen. It is difficult on frozen section of metastases in lymph nodes to see the fine cellular detail and staining properties which differentiate primary thyroid carcinoma from metastatic disease primary elsewhere. It is even difficult on permanent section, particularly in metastases from certain tumors of the breast and the clear cell tumors of the kidney. This applies to sections of the tumor in the thyroid as well as to the metastases.

Obviously every thyroid nodule should be approached with doubt as to its nature. The more doubt, the more equivocal the preoperative diagnosis. In hindsight, in all of these cases, it appears that there was something not wholly classical in the disease in the neck. This fact was appreciated in most of them by at least one physical examiner before operation.

We believe that the removal of part or all of the thyroid gave palliation in a number of our cases and was mandatory in some. In our opinion, the slow course of "hypernephroma" warrants an aggressive policy of attack on the metastases. It has been of great interest to us that after radical thyroid operations for metastatic disease there have been no recurrences in the cervical region, although in every case the carcinoma was the main contributing cause of death and was usually widely disseminated.

Conclusions

The clinician should be alert to the possibility of this "masquerade" of metastatic carcinoma in the thyroid gland, and so should the surgical pathologist.

If a thyroid nodule is suspected of being metastatic, the breasts, kidneys, and lungs should be the first organs investigated.

Unfortunately, primary cancer of breast and kidney can be deceptively silent, and x-ray interpretation of pulmonary nodules misleading.

Our main conclusion, therefore, in which we seem to be in accord with Cope and associates,¹² is that there are indeed "dangerous thyroid nodules." At times we have wondered whether there are any safe ones.

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